

REMARKS

This Amendment is filed in response to the final Office Action dated September 21, 2005. For the following reasons this application should be allowed and the case passed to issue. No new matter is introduced by this Amendment. The amendments to the specification correct informalities. The amendments to the claims are supported by the specification and claims as originally filed. New claim 16 is supported by originally filed claim 12.

Claims 1, 4-11, 13, and 16 are pending in this application. Claims 1, 2, 4-11, and 13 have been rejected. Claims 1, 7, 8, 9, 10, and 13 have been amended in this response. Claim 2 was canceled in this response and claims 3, 12, 14, and 15 were previously canceled. New claim 16 has been added.

Claim Rejections Under 35 O.K. § 103

Claims 1, 2, 5-11, and 13 were rejected under 35 O.K. § 103(a) as being unpatentable over Monzyk (U.S. Pat. No. 5,304,382) in view of Buchwalter et al. (U.S. Pat. No. 4,102,863). This rejection is traversed, and reconsideration and withdrawal thereof respectfully requested. The following is a comparison of the invention, as claimed, and the cited prior art.

An aspect of the invention, per claim 1, is a method of the production of a nanoparticle which comprises a step of forming a nanoparticle including a hydroxide of a metal ion in a cavity part of a protein by mixing a first solution and a second solution. The first solution contains a protein having a cavity part inside, an alkaline buffer solution, and a metal ion selected from the group consisting of a nickel ion (Ni^{2+}), a chromium ion (Cr^{2+}) and a copper ion (Cu^{2+}). The second solution contains carbonate ion and/or carbonate ion.

The Examiner asserted that Monzyk discloses nanoparticles prepared by combining an apoferritin protein shell together with metal ions or other chemical entities such as carbonate and

mixtures of hydroxides and oxides in a solution. The solution can be buffered with HEPES or ammonium acetate. After formation of the nanoparticle, the protein can be eliminated by the addition of heat. The Examiner acknowledged that Monzyk does not teach forming carbonate ions by bubbling carbon dioxide. The Examiner relied on the teaching of Buchwalter et al. of bubbling carbon dioxide in solution of water to form carbonate ions to assert that it would have been obvious to bubble carbon dioxide in a water solution to form the carbonate ions.

Buchwalter et al. and Monzyk do not suggest the claimed method of the production of a nanoparticle because there is insufficient motivation to combine Buchwalter et al. and Monzyk, as asserted by the Examiner. Buchwalter et al. and Monzyk are directed to non-analogous technologies. Monzyk is directed to forming aluminum nanoparticles, while Buchwalter is directed to the electrodeposition of ionic resins.

"In order to rely on a reference as a basis for rejection of applicant's invention, the reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the inventor was concerned." *In re Oeticker*, 977 F.2d 1443, 1446, 24 USPQ2d 1443, 1445 (Fed. Cir. 1992). Buchwalter et al. is neither directed to the field of Applicants' endeavor, forming a nanoparticle, nor pertinent to the problem with which Applicants were concerned, forming nanoparticles having a uniform diameter. One of ordinary skill in the art of forming metallic nanoparticles would not be motivated to look at a teaching of electrodepositing ionic resins to solve a problem in nanoparticle formation.

Even if there was sufficient motivation to combine Buchwalter et al. with Monzyk, and Applicants do not believe there is, the claimed method would still not be obvious in view of Monzyk and Buchwalter et al. Merely mixing nickel ion, chromium ion, or copper ion with hydroxide to form nickel hydroxide, chromium hydroxide, or copper hydroxide in apoferritin

generates an insufficient yield of metal hydroxide (about 20%). The addition of carbonate ions or hydrogen carbonate ions dramatically improves the yield to nearly 100%.

Monzyk discloses that salts of cations and anions are formed in apoferritin (column 4, line 52 to column 5, line 15). As disclosed by Monzyk, a cation (e.g. aluminum ion) of a desired salt (e.g. aluminum nitrate and aluminum hydroxide), is mixed with an anion (e.g. nitrate ion and hydroxide ion) of the salt desired to obtain the desired salt (e.g. aluminum nitrate and aluminum hydroxide). Monzyk discloses forming metal hydroxide in apoferritin by mixing metal ion and hydroxide ion in solution. However, as shown in Table 6 and 7 (page 27) of the present specification, the yield of nickel hydroxide is only at most 20% when nitrogen or oxygen is bubbled in a solution at a pH of 8.2 to 8.4. On the other hand, when mixing a metal ion and hydroxide ion (the hydroxide ion is contained in an alkaline buffer solution) with carbonate ion or hydrogen carbonate ion, according to the claimed invention, the metal hydroxide yield is nearly 100% (See Table 5, page 26).

Thus, when nickel hydroxide, chromium hydroxide, or copper hydroxide is produced using a protein having a cavity part inside, a dramatic improvement in yield is obtained by mixing carbonate ion or hydrogen carbonate ion in the reaction solution. This unexpected improvement in yield is not suggested by Monzyk or Buchwalter et al.

Claim 4 was rejected under 35 U.S.C. § 103(a) as being unpatentable over Monzyk in view of Buchwalter et al. and further in view of JP 2001-504277 (JP '277). This rejection is traversed, and reconsideration and withdrawal thereof respectfully requested.

The Examiner acknowledged that Monzyk in view of Buchwalter et al. do not teach a method of inserting nickel ion into the cavity of a protein. The Examiner relied on the JP '277 teaching of forming nickel nanoparticles using apoferritin to assert that it would have been

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obvious to incorporate nickel ions in apoferritin to produce nanoparticles with ferromagnetic properties.

The combination of JP `277 with Buchwalter et al. and Monzyk does not suggest the claimed method because JP `277 does not cure the deficiencies of Buchwalter et al. and Monzyk, as explained above. Therefore, claim 4 is allowable for at least the same reasons as independent claim 1.

In light of the above Amendment and Remarks, this application should be allowed and the case passed to issue. If there are any questions regarding these remarks or the application in general, a telephone call to the undersigned would be appreciated to expedite prosecution of the application.

To the extent necessary, a petition for an extension of time under 37 C.F.R. § 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 500417 and please credit any excess fees to such deposit account.

Respectfully submitted,

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